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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,325	02/16/2006	Shailesh Bhamare	SMC-PT004	2977

3624 7590 02/21/2008

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
02/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,325	BHAMARE ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 - 11, 13, 14, 16, 17, 19 - 26 and 28 - 31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 - 11, 13, 14, 16, 17, 19 - 26 and 28 - 3 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/16/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1 – 11, 13, 14, 16, 17, 19 – 26 and 28 – 31 are pending and currently under examination.

Specification

1. The use of the trademark "Pharmatose" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1 – 3, 5 – 9, 16, 17 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30, 37, 39 and 40 of copending Application No. 10/495,961. Although the conflicting claims

are not identical, they are not patentably distinct from each other because they both recited compositions of overlapping ingredients.

The claims of the instant application require a cephalosporin antibiotic, of which beta-lactam antibiotic are included and the presence of at least two carbomers that are hydrophilic polymers that result in the controlled release of the antibiotic. Ingredients that can be added the pharmaceutical composition include the lubricant calcium stearate.

The claims of the copending Application '961 require a beta-lactam antibiotic, a hydrophilic polymer and a stabilizing amount of one or more calcium salts to form the controlled release matrix of a pharmaceutical composition. Calcium stearate is a pharmaceutically acceptable calcium salt that may be included as a stabilizer (Application '961) or as a lubricant (the instant Application).

The claims of the two compositions encompass pharmaceutical compositions with the same ingredients although those ingredients are described in terms of different functions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 1, 2, 9, 10, 12, 14, 16, 17, 21, and 28 – 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 10 – 15 and 17 – 19 of copending Application No. 11/579,988. Although the conflicting claims are not identical, they are not patentably distinct from

each other because the encompass pharmaceutical compositions of the same ingredients.

The claims of co-pending application claim a pharmaceutical composition of cefixime, a cephalosporin antibiotic, with a particular particle size that leasds to a composition that is bioequivalent to a suspension of cefixime trihydrate. Various bases and excipients can be included in the pharmaceutical composition.

The claims of the instant application require a cephalosporin antibiotic such as cefixime and at least two carbomers. Various pharmaceutical excipients can be added to the pharmaceutical composition. The carbomers required in the instant application could be present in the composition of the copending Application to achieve the claimed bioequivalent drug release profile of the pharmaceutical formulation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim recites limitations regarding the C_{max} of the delayed release form and compares it to that of an immediate release formulation. However, the release profile and C_{max} of the immediate release form is not provided so what values of C_{max} would be required are not described.

Claim Rejections - 35 USC § 112 2nd Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6 and 8 contains the trademark/trade name CARBOPOL 971P® and CARBOPOL 974P®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the carbomers used in the controlled

release pharmaceutical composition and, accordingly, the identification/description is indefinite.

7. Claims 10, 13 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims contain a list of possible ingredients that an ingredient can be selected from that concludes with "and the like." This renders the list of ingredients from which one item must be selected vague and indefinite since no definition of "the like" is included.

8. Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims introduce a limitation with the word "preferably". It is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

9. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "substantially the same as" in claim 25 is a relative term which renders the claim indefinite. The term "substantially the same as" is not defined by the claim, the specification does not provide a standard for ascertaining the

requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1 – 11, 13, 14, 16, 17, 19 – 26 and 28 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kshirsagar et al. (WO 2004/019901, cited on PTO-1449).

Kshirsagar et al. discloses sustained release pharmaceutical compositions of beta lactam antibiotics or their pharmaceutically acceptable salts, hydrates or esters (p 1, ln 4 – 7). In this therapy, it is desirable to maximize the blood concentration of the drug at several fold above the minimum inhibitory concentration (MIC) while minimizing the risk of toxicity and anti-microbial resistance to the drug (p 1, ln 20 – 24). Polymer blends are known and frequently used in the art in sustained release composition because the ability to blend different polymers in different ratios can create different release properties (p 10, ln 7 – 11).

In the compositions prepared by Kshirsagar et al., the antibiotic comprises about 25% to 90% by weight of the composition (p 12, ln 1 – 3). The mixture of polymers comprises about 1% to 35% by weight of the composition (p 12, ln 4 – 6). The tablets are prepared by a process in which the active ingredients, excipients and polymer ingredients are combined, the blended material is compacted to produce granules and then those granules are compressed to form a tablet (p 14, ln 1 – 14). Antibiotics that are suitable for use in these compositions include cefpodxime proxetil, cefuroxime axetil, cefprozil, cefadroxil, cefamandole, cefoxitin, cefalothin and cephapirin (p 14, ln 16

– 21). The addition of lactose to the composition resulted in a controlled, uniform release of the antibiotic over time (p 16, ln 10 – 13). A combination of polyacryclic acid derivatives such as CARBOPOL® 971P and CARBOPOL® 974P is disclosed as ingredients that can enhance the integrity of the composition (p 16, ln 25 – 28). The presence of water soluble and water dispersible diluents such as mannitol, glucose, sorbitol, maltose, dextrans, dextrins, microcrystalline cellulose and pre-gelatinized starch is also disclosed (p 17, ln 1 – 9). Lubricants such as talc, stearic acid, magnesium stearate and colloidal silicon dioxide may also be present in the pharmaceutical compositions (p 17, ln 10 – 13).

In the examples provided, the amount of cefpodoxime proxetil was 537 mg, although this is equivalent to 400 mg of cefpodoxime (ex 1, p 19). This composition also contained 15.08% by weight of anhydrous lactose and 1.06% by weight of the lubricant magnesium stearate but only 7.05% by weight of calcium carboxymethyl cellulose, used as a water dispersible diluent that is functionally equivalent to microcrystalline cellulose. In example 12 (p 28), however, the amount of this ingredient is higher (27.66% by weight).

The references do not specifically teach the C_{max} and T > MIC of the composition as claimed by Applicant. These parameters are clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal C_{max} and T > MIC to best achieve the

desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of C_{max} and T > MIC would have been obvious at the time of Applicant's invention.

The references do not specifically teach the amount of the multiple CARBOPOL® polymers in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Therefore the claims of the instant application are rendered obvious to one of ordinary skill in the art at the time of the instant invention by the teachings of Kshirsagar et al.

14. Claims 1 – 9, 13, 14, 16, 17, 19 – 26, and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katzhendler et al. (US Patent 6,399,086) in view of Mayron (US Patent 3,074,852).

Katzhendler et al. discloses controlled release oral drug delivery systems with beta-lactam antibiotics as the active ingredient (col 3, ln 32 – 34). Among the

cephalosporins that are exemplified as being suitable for these compositions is cefprozil (col 4, ln 11 – 25). The amoxicillin compositions prepared in example 3 contain about 16% by weight of polymer, about 0.01% of the lubricant magnesium stearate, about 0.01% by weight of the lubricant silicon dioxide (AEROSIL®) and about 7% of the binder microcrystalline cellulose (AVICEL®). They contain about 600 mg of the active ingredient, comprising about 75% of the formulation. Granules of the antibiotic and polymer can be compressed into tablets (col 5, ln 65 – col 6, ln 2).

Katzhendler et al. does not disclose the use of carbomer(s) as a polymeric material that is suitable as a delayed release polymer.

Mayron discloses delayed (controlled) release therapeutic compositions and methods for preparing them (col 1, ln 9 – 12). Carboxy vinyl polymers such as the CARBOPOL® polymers are exemplified as suitable polymers for use in such controlled release pharmaceutical compositions (col 2, ln 11 – 23). Drugs that can be included in the controlled release pharmaceutical formulations include antibiotics (col 3, ln 1) such as penicillin (col 4, ln 46 – 55), a beta-lactam antibiotic. In that composition, about 46% by weight of the composition is CARBOPOL® 934. In example 2 (col 4, ln 12 – 24), a sustained release preparation is prepared using a 1:1 mixture of CARBOPOL® 940 and CARBOPOL® 941. Well known excipients and binders and lubricants such as magnesium stearate or talc can be included in the tablets (col 3, ln 34 – 38). The amount of lubricant present with the carboxy vinyl (carbomer) polymer is about 0.5% (col 3, ln 55 – 56).

Katzhendler et al. teaches the desirability of delayed release pharmaceutical dosage forms of antibiotics such as cefprozil. Mayron teaches that a combination of CARBOPOL® polymers can be used to produce a controlled release pharmaceutical formulation. The various CARBOPOL® polymers have similar structures and it is within the skill of one of ordinary skill in the art to substitute various carbomer polymers with different characteristics to achieve the desire release profile.

The references do not specifically teach the C_{max} and T > MIC of the composition as claimed by Applicant. These parameters are clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal C_{max} and T > MIC to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of C_{max} and T > MIC would have been obvious at the time of Applicant's invention.

The references do not specifically teach the dosage in milligrams of the cefprozil claimed by Applicant. These parameters are clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal dosage of cefprozil to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed

parameters, this optimization of the dose of the cefprozil would have been obvious at the time of Applicant's invention.

As to the presence and amounts of the other ingredients, the combined teachings of Katzhendler et al. and Mayron meet the limitations put forth by Applicant. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). **MPEP 2144.05**.

Therefore the claims of the instant application were obvious to one of ordinary skill in the art at the time of the instant invention in light of the combined teachings of Katzhendler et al. and Mayron.

15. Claims 1, 10, 11 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katzhendler et al. and Mayron as applied to claims 1 – 9, 13, 14, 16, 17, 19 – 26, and 29 – 31 above, and further in view of Patel et al. (US Patent 6,248,363).

As discussed above, Katzhendler et al. and Mayron teach a delayed release formulation of a beta-lactam antibiotic such as cefprozil. The delayed release polymer used can be a combination of carbomer polymers such as the CARBOPOL® series of polymers. Katzhendler et al. and Mayron do not teach the inclusion of lactose or other diluents in the solid delayed-release pharmaceutical formulations.

Patel et al. discloses solid pharmaceutical compositions of a wide variety of active ingredients (col 1, 7 – 12). Diluents such as lactose, mannitol, talc and sorbitol

are disclosed as additives that are conventionally added to pharmaceutical compositions (col 39, ln 10 – 13; col 40, ln 23 – 29).

The references do not specifically teach adding the diluent such as lactose in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of diluent to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to add a diluent such as lactose to the delayed release beta-lactam antibiotic composition taught by Katzhendler et al. and Mayron.

Conclusion

Claims 1 – 11, 13, 14, 16, 17, 19 – 26 and 28 – 31 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER